UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/566,121 | 01/25/2006 | Bruce E. Reidenberg | 02755/100J539-US1 | 3707 |

7278 7590 09/25/2009

DARBY & DARBY P.C.
P.O. BOX 770
Church Street Station
New York, NY 10008-0770

| EXAMINER | |
|---|---|
| YOUNG, MICAH PAUL | |
| ART UNIT | PAPER NUMBER |
| 1618 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 09/25/2009 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/566,121 | REIDENBERG ET AL. | |
| | Examiner | Art Unit | |
| | MICAH-PAUL YOUNG | 1618 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/25/06, 1/04/07, 8/10/07, 10/06/08, 8/18/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Information Disclosure Statement*

The information disclosure statements (IDS) submitted on 1/25/06, 1/4/07, 8/10/07, 10/06/08 and 8/18/09 were filed in a timely fashion. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 4, 5, and 13-15 are rejected under 35 U.S.C. 102(a) as being anticipated by Lintzeris et al (*Buprenorphine dosing regime for inpatient heroin withdrawal: a symptom-triggered dose titration study*, Drug and Alcohol Dependence, 70 (2003) 287-297).

The Lintzeris study teaches a method of treating withdrawal symptoms in heroin addicted patients comprising a titration where the patients were dosed in several separate dosing periods with different concentrations of transdermal buprenorphine formulations (Abstract). The subjects were given a dosage of buprenorphine on the first day of the trial, 87% of the subjects were given a second dosage the next day, while 62% required further dosing for an additional 3 days (page 390, 3.4). The dosages for the entire 5 day study varied, but in general tapered off as symptoms waned (Table 2 and Fig. 1). The recommended dosing regimen is such that a patient can receive as low as 4 mg of buprenorphine the first day at the onset of withdrawal symptoms

and a second dosage of at a separate time of an additional 4 mg. The initial dosing period would be at the onset of symptoms with the second dosing period later that day with the onset of further symptoms. The third dosing period would last for at least the remainder of the five day study with a total of 10 mg of buprenorphine administered (Table 3).

Regarding the plasma concentration of the patient after administration of the third dosing period, it is the position of the Examiner that this limitation is merely functional limitation that would fall naturally from the compositional components of the method. As discussed above the Lintzeris study teaches a dosing regimen describing three separate and distinct dosing periods with the dosage of buprenorphine sublingual tablets, staying the same in the second period and increasing throughout the third period. These disclosures meet the compositional components of the instant claims and as such would meet the functional limitations of the claims.

These disclosures render claims anticipated.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Fischer et al (*Treatment of opioid-dependent pregnant woman with buprenorphine*; Addition (2000) 95(2), 23-244).

The Fischer study teaches a method of treating opioid-dependent pregnant women with a transdermal dosage of buprenorphine (Abstract). The pregnant women were required to be healthy and were administered transmucosal tablets of buprenorphine (page 240 col. 2). Withdrawal symptoms were monitored in the woman as well as neonatal abstinence syndrome in the children upon birth (page 241-page 242). These disclosures render the claims anticipated.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 and 4-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Lintzeris et al (*Buprenorphine dosing regime for inpatient heroin withdrawal: a symptom-triggered dose titration study*, Drug and Alcohol Dependence, 70 (2003) 287-297) in view of Granger (EP 0 432 945 hereafter '945).

As discussed above the Lintzeris study discloses a method of treating withdrawal symptoms in heroin addicted patients comprising a titration where the patients were dosed in several separate dosing periods with different concentrations of transdermal buprenorphine formulations (Abstract). The reference is however silent to subsequent administrations of buprenorphine for withdrawal treatment. The study does however identify a segment of the subjects that did not complete the study and as such would be prone to further withdrawal

symptoms later on and require a subsequent administration. The administered of a subsequent dosage form such as described in the '945.

The '945 patent discloses a transdermal buprenorphine dosage form comprising from 0.25-100 mg of buprenorphine (abstract, page 2, lin. 49-52). The dosage form results in a blood plasma level from 0.6-6 ng/ml (page 3, lin. 40-48). The transdermal dosage from include all manners of topical and transdermal dosage forms including lotions, gels, sprays, creams, films, and patches (***Ibid.***). The transdermal dosage forms would provide an effective treatment maintaining constant blood levels, effective to reduce withdrawal symptoms of cocaine or heroin addiction. It would have been obvious to dose the patients of the Lintzeris study with the constant stable transdermal formulation of the since the oral and sublingual dosages would only provide immediate relief of symptoms and the transdermal dosage forms would provide prolonged relief and reduce chances of relapse.

Regarding the dosing of the separate dosing periods, the Lintzeris study reports slightly lower concentrations of 4-8 mg being administered. However the study indicates that dosing concentration is dependent on the patient and the severity of their symptoms, meaning that patient with more severe withdrawal symptoms and a longer or more sever history of opioid addiction would require a higher dosage, specifically women require higher concentrations of buprenorphine (page 292 col. 2). With these things in mind it would have been obvious to increase the concentration of the buprenorphine during the treatment period in order to meet the symptom needs of the patient.

With these things in mid it would have been obvious to additionally treat withdrawal patients with a transdermal formulation that maintains a constant blood plasma level, after an

oral regimen in order to reduce chances of relapse. One of ordinary skill in the art would have been motivated to combine the prior art in order to properly and more effectively treat withdrawal symptoms. It would have been obvious to treat withdrawal patients in need thereof as such with an expected result of a treatment regimen that provides improved long term results with reduced incidence of relapse.

***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICAH-PAUL YOUNG whose telephone number is (571)272-0608. The examiner can normally be reached on Monday-Friday 8:00-5:30; every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

/MICAH-PAUL YOUNG/
Examiner, Art Unit 1618